c.) REMARKS

Original claims 1-8 were previously cancelled. By this paper, claims 9, 12, 14, 15, 17, 19 and 20 are amended, claim 16 is cancelled, and new claims 21 and 22 are added.

The amendments to claims 9, 12, 15, 17, 19 and 20 are merely clarifying in nature and do not alter the scope of the claims. The unnecessary verbiage "surface protein antigen" has been deleted from claims 9, 12 and 19; the article "of" has been replaced with the more appropriate "from" in claims 12 and 19; the term "antigen" has been replaced by "recombinant MSP1a" in claim 15 to accord with the change to claim 9; and the phrase "of said vaccine composition" has been inserted into claims 17, 19 and 20 to provide better context for the term "immunogen".

In response to the noted § 112 objection, claim 14 has been amended to change its dependency from cancelled claim 1 to pending claim 9.

New claim 21 comprises cancelled claim 16 with the dependency changed from claim 15 to 17 and further specifies that the dose includes the recited amount of tick cell culture derived *A. marginale*. The claim is supported in the specification at p. 10, lines2-4, among other places.

New claim 22 depends from claim 9 and further provides that the recombinant MSP1a is associated to *E. coli* membrane fractions. Support for the claim can be found at p. 19, lines 8-10, of the specification.

§ 102(b) Rejection

The examiner rejected claims 9, 12-15, 19 and 20 under 35 U.S.C. 102(b) as being anticipated by McGuire et al. (USPN 5,549,898) in light of McGarey et al., 1994 (*Infection and Immunity*, 62/10:4587-4593), stating:

> McGuire et al discloses a purified antigenic surface protein of *A. marginale* and that the antigen is useful as a vaccine component for protecting mammals against infection by *A. marginale* (abstact; col. 1; col. 6; col. 17; claims). This protein has a molecular weight of 105 kD (figures; col. 2; col. 4). The protein has been produced by recombinant DNA techniques (cols. 4-8). McGuire et al disclose that the vaccine also contains adjuvants or any other suitable pharmaceutically acceptable carrier or diluent. (col. 8). McGuire et al discloses other antigenic (i.e. immunogen from *A. marginale*) and those [sic] they are also of use (col. 4). McGuire et al disclose that in addition to the native proteins isolated and purified from *A. marginale*, the antigens and immunogens according to this invention can comprise active agents formed of one or more such proteins, polypeptide fragments of such proteins, or one or more immunologically similar proteins or polypeptides produced by synthesis or genetic engineering (col. 4). McGuire et al indicate that purified antigens can be made by recombinant means or artificially synthesized (col. 6). McGuire et al disclose the use of Oklahoma isolates (col. 18).

The abstract of McGarey is cited by the examiner to show that MSP1a has a molecular weight of 105 kD, presumably to relate the McGuire et al disclosure to Applicant's claimed invention.

This rejection is respectfully traversed.

For starters, McGuire et al. is about the immunogenicity of purified MSP1 complex. The patent teaches that purified MSP1 complex may be sufficient as a vaccine to impart protective immunity against *A. marginale*; but, by its own admission, the patent fails to demonstrate the immunogenicity of either native or recombinant MSP1a. Consider first the following excerpt from McGuire et al., which establishes the correspondency of MSP1 complex to McGuire et al.'s protein designated "Am105"; MSP1a to Am105U; and MSP1b to Am105L.

> The two [MSP] proteins as a complex are herein sometimes referred to as Major Surface Protein 1 (MSP-1) as well as the term Am105. The two proteins which make up the doublet are herein referred to as Am105U and Am105L. **The protein Am105U is also sometimes referred to as MSP-1a with the Am105L sometimes referred to as MSP-1b**. (col. 13, lines 15-20) (emphasis supplied).

McGuire et al.'s reported immunization studies involved only the purified MSP1 complex (Am105) (col. 17, lines 8-51). Notably, only five Am105 vaccinates were studied, and, of the five, only two attained complete protection.

The examiner cites McGarey to show that the 105kD protein discussed in McGuire et al. must be MSP1a. However, McGuire et al. explicitly discloses that the purified MSP1 complex itself has a molecular weight of 105 kD.

> The purified Am105 has a molecular weight of about 105,000 daltons as measured by electrophoretic mobility analysis.... (col. 6, lines 22-24).

While McGuire et al. reports the synthesizing of recombinant MSP1 (Am105), it concludes that there are important antigenic differences between the purified and recombinant MSP1.

> Recombinant Am105 was recognized by R873 and hence was antigenically homologous with Am105U and/or Am105L polypeptides. However, recombinant Am105, expressed by any of the recombinants, was not recognized by monoclonal antibodies $22B_1$ or $15D_2$ in immunoprecipitation or immunoblot assays (data not shown), or by R781 (FIG. 3, lanes 2 and 13). **There were, therefore, important antigenic differences between recombinant and native Am105**. (col. 24, lines 4-12) (emphasis supplied).

McGuire et al. actually identifies its recombinant MSP1 protein (Am105) to be homologous, and possibly identical, to native **MSP1b** (Am105L) (col. 24, lines 3-4, 34-41). In contrast, cleavage

peptidesof native MSP1a (Am105U) were found to be largely dissimilar to both MSP1b (Am105L) and recombinant MSP1 (Am105). (col. 24, lines 42-44).

Significantly, McGuire et al. admits a lack of any evidence supporting structural or antigenic homology between recombinant MSP1 (Am105) or MSP1b (Am105L), on the one hand, and MSP1a (Am105U).

> Recombinant Am105 is structurally and antigenically homologous to Am105L. No evidence was obtained for structural or antigenic homology between recombinant Am105 and Am105U polypeptides or between Am105L and Am105U. (col. 25, lines 36-40).

McGuire et al. concludes:

> Nonrecombinant Am105, containing both Am105L and Am105U, confers protection on cattle against challenge with Anaplasma marginale (17). **It is not known whether Am105L or Am105U, used separated as an immunogen, would confer protection**. (col. 26, lines 38-42) (emphasis supplied).

Thus, it is clear that McGuire et al. does not anticipate Applicant's claimed invention. By its own admission, McGuire et al. presents absolutely no evidence that either nonrecombinant MSP1a or recombinant MSP1a is, or would be, an effective immunogen. Indeed, McGuire et al. is constrained by the reported test results even to conclude that the recombinant MSP1 *complex* is effective for conferring protection. McGuire et al. points to the need for further research in this regard:

> Experiments in progress examine whether recombinant Am105 will induce protection in cattle against disease and whether Am105U may be expressed in E. coli so that both components of the Am105 complex may be tested for protection. (col. 27, lines 5-9).

Applicant's claimed invention encompasses a vaccine composition against *A. marginale* including recombinant MSP1a in combination with an immunogen derived from *A. marginale* and a carrier or diluent, as well as a method for inducing protective immunity using the composition. Considering the lack of any disclosure in McGuire et al. that the administration of full length recombinant MSP1a imparts protective immunity, and further in light of the extensive explicit disclosure of McGuire et al. as relates to the uncertainty and unpredictability between the native and recombinant MSP1 investigated, the patent cannot be said to provide a reasonable expectation of success that recombinant MSP1a would be effective in conferring protection against *A. marginale*. The patent thus fails to enable the use of recombinant MSP1a as a vaccine against *A. marginale*, and, as such, the reference is insufficient to anticipate the claimed invention. See *In re Sun*, 31 USPQ2d 1451, 1453 (Fed. Cir. 1993) (unpublished) ("But to be prior art under section 102(b), a reference must be enabling.... That is, it must put the claimed invention in the hand of one skilled in the art.").

For at least the foregoing reasons, reconsideration of the examiner's 102(b) rejection is respectfully solicited.

§ 103(a) Rejection

Claims 10, 11 and 16 [sic, should be 17]-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over McGuire et al. (USPN 5,549,898) in light of McGarey et al., 1994 (*Infection and Immunity*, 62/10:4587-4593) as applied to claims 9, 12-15, 19 and 20 above, and further in view of Barbet et al. 1999. The examiner reiterated McGuire et al. as disclosing the claimed invention except for the immunogen being tick cell culture derived *A. marginale*. Barbet et al. is cited for teaching tick cell culture derived *A. marginale*. The examiner concludes that:

> [I]t would have been obvious to a person of ordinary skill in the art at the time the invention was made to use both the isolated MSP1a antigen and other immunogens even the tick cell culture since the art teaches that the antigenic proteins are on the cell surface.

This rejection is also respectfully traversed.

The deficiencies of McGuire et al., as detailed above, are left uncured by the combination with Barbet et al., which merely regards the propogation of *A. marginale* in tick cell culture. Thus, for similar reasons the noted combination fails to render the claimed invention *prima facie* obvious.

In addition, and as further ground for allowance of claims 10-11 and 17-18, Applicant would direct the examiner's attention to FIG. 2 and page 13 of the specification, wherein it is reported that the combination of recombinant MSP1a and tick cell derived antigens significantly reduced PCV in cattle to a degree not achieved by all other tested vaccine preparations, save erythrocyte-derived antigens. Neither recombinant MSP1a nor tick cell derived *A. marginale*, administered alone, resulted in the level of protection obtained using the combination of both. This surprising finding is not described in the cited references and is otherwise fully sufficient to support patentability related to these claims irrespective of the noted rejection.

* * * * *

Considering the foregoing, it is sincerely believed that this case is in a condition for allowance, which is respectfully requested.

This paper is intended to constitute a complete response to the outstanding Office Action. Please contact the undersigned if it appears that a portion of this response is missing or if there remain any additional matters to resolve. If the Examiner feels that processing of the application can

be expedited in any respect by a personal conference, please consider this an invitation to contact the undersigned by phone.

Respectfully submitted,

4/5/04
DATE

SIGNATURE OF PRACTITIONER

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